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VIKSNINS HARRIS & PADYS PLLP
P.O. BOX 111098
ST. PAUL, MN 55111-1098

EXAMINER	
WESSENDORF, TERESA D	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/903,412
Filing Date: July 11, 2001
Appellant(s): KOIDE, SHOHEI

Peter L. Malen
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/20/2011 appealing from the Office action mailed 3/30/2010.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related

to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Appeal No. 2009-1912 of the instant application was decided on 6/9/2009, reopening prosecution of the instant application based on the new grounds of rejection made by the Board.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1, 4, 7-8, 55-57, 59-64, 66-78 and 80-82.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after non-final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being

maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

6,818,418	LIPOVSEK	11-2004

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 4, 7-8, 55-57, 59-64, 66-78 and 80-82 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lipovsek.

The Board in their decision made on 6/9/09 starting at page 10, states:

Lipovsek teaches an alignment of Fibronectin type III sequences in Figure 4, which identify the locations of positions 7, 9 and 23 on the Fibronectin type III molecule. (Please see

Figure 4 sequence alignment at page 10 of the decision). "FIG. 4 is a graph illustrating a sequence alignment between fibronectin type III protein domain and related protein domains" (Lipovsek, col. 6, lines 31-33). Lipovsek teaches a Canis familiaris (Cf) sequence which is a Fibronectin type III molecule with a substitution of Asp 7 by neutral Asparagine, a substitution of Glu 9 by positively charged Arginine and a substitution of Asp 23 by Glutamine relative to the wild type human Fibronectin type III sequence (see Lipovsek, Figure 4, 8th line ("Cf") in alignment; FF 16). Lipovsek teaches another sequence, RN, in which the Fibronectin type III molecule has a substitution of Asp 23 for Glutamic acid relative to the human fibronectin wild type sequence (see Lipovsek, Figure 4, 3rd line in alignment; FF 16). Lipovsek teaches another sequence, HS CAP, in which the Fibronectin type III molecule has a substitution of Glu 9 by asparagine relative to the human fibronectin wild type sequence (see Lipovsek, Figure 4, 13th line in alignment; FF 16).

Principles of Law "[T]he PTO gives a disputed claim term its broadest reasonable interpretation during patent prosecution". In re Bigio, 381 F.3d 1320, 1324 (Fed. Cir. 2004). The court recognizes the fairness of reading claims broadly "before a patent is granted [since] the claims are readily amended as part of the examination process." Burlington Indus. v. Quigg, 822

F.2d 1581, 1583 (Fed. Cir. 1987). "Thus, a patent applicant has the opportunity and responsibility to remove any ambiguity in claim term meaning by amending the application". Bigio, 381 F.3d at 1324. Applying the broadest reasonable interpretation to claims also "serves the public interest by reducing the possibility that claims, finally allowed, will be given broader scope than is justified." In re Am. Acad. of Sci. Tech. Ctr., 367 F.3d 1359, 1364 (Fed. Cir. 2004).

The Specification does not directly define "modified" but discloses that a "stabilizing mutation is defined herein as a modification or change in the amino acid sequence of the Fn3 molecule, such as a substitution of one amino acid for another" (Spec. 6, 11. 20-24). Also, the Specification states that "[o]ne or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3" (Spec. 7, 1ines 6-8). Therefore, the word "modified" is reasonably interpreted in light of the Specification as representing a Fibronectin type III molecule in which there are one or more changes or substitutions in the amino acid sequence relative to the human wild type sequence. Dependent claims 4 and 7 specifically identify replacement of Asp 7 or Asp 23 with asparagine as a mutation within the scope

of claim 1 (see claims 4 and 7). Lipovsek teaches a human Fibronectin type III sequence which is identical to that disclosed in the Specification (FF 16-17). Lipovsek also teaches Fibronectin type III sequences which are "modified" relative to the human sequence (FF 18-19). Specifically, Lipovsek teaches a Canis familiaris (Cf) sequence which is a Fibronectin type III molecule with a substitution of Asp 7 by Asparagine, a mutation of Glu 9 by Arginine and a substitution of Asp 23 by Glutamine relative to the wild type human FND (Fibronectin type III domain) sequence among other sequence differences (see Lipovsek, Figure 4, 8th line in alignment; FF 17- 18). Lipovsek also teaches another sequence, RN, in which the Fibronectin type III molecule has a substitution of Asp 23 by Glutamic acid relative to the human FND wild type sequence (see Lipovsek, figure 4, 3rd line in alignment; FF 17, 19). Lipovsek also teaches another sequence, HS CAP, in which the Fibronectin type III molecule has a substitution of Glu 9 by asparagine relative to the human FND wild type sequence (see Lipovsek, Figure 4, 13th line in alignment; FF 17, 20). The Cf, RN, and HS CAP sequences are reasonably interpreted as modified Fibronectin type III molecules with substitutions which would reasonably be believed as inherently stabilizing based upon the teachings of the Specification (FF 12-14). With regard to claims 4, 55, 57, 59,

61, and 63, Lipovsek teaches the Cf Fibronectin type III sequence with a neutral asparagine at the position of Asp 7 (FF 18). With regard to claims 7, 8 and 57, Lipovsek teaches both the Rn and Cf Fibronectin type III sequences with substitutions of one other amino acid residue at Asp 7, Asp 23, and Glu 9 (FF 18-19). With regard to claim 56, Lipovsek teaches a Cf Fibronectin type III sequence in which the Glu 9 is substituted with a positively charged arginine residue (FF 18). With regard to claims 55 and 59-60, Lipovsek teaches a Cf Fibronectin type III sequence in which the Asp 23 is substituted with a neutral glutamine residue (FF 18). With regard to claim 62, Lipovsek teaches a Hs CAP Fibronectin type III sequence in which the Glu 9 is substituted with asparagine (FF 20). In particular regarding the functional requirement that the mutation is a "stabilizing" mutation, we find that since the mutations disclosed by Lipovsek are identical to those required by the claims, the mutations would reasonably be expected to inherently function as "stabilizing" mutations in the absence of evidence to the contrary (FF 16-19). See In re Spada, 911 F.2d 705,708 (Fed. Cir. 1990) ("[W]hen the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.") The claimed substitution of Asp7 and 23 and Glu9

with neutral or positively charged residues with Arg at position 6 (claims 1 and 57) and Asp 7, 23 with the positively charged residues (claim 80) are anticipated or obvious over Lipovsek with the above substitutions and as expounded in the responses below. Alternatively, the present claims which recites a modified human FN3 or 10FN3 with substitution in at least one of Asp7,23 or Glu9 with a neutral or positively charged (claims 1 and 57) and Asp,7, 23 with positively charged residue(claim 80) is obvious over Lipovsek as explain more in detail below.

(10) Response to Argument

Appellant notes that in Appeal 2009-1912, the Board rejected the then pending claims only under 35 U.S.C. § 102(e), not under 35 U.S.C. § 103(a) (see pages 8 and 14 of the decision).

In reply, as appellant acknowledged the decision by the Board was with then pending claims and not with the presently amended claims.

Claims 1 and 57

Appellant acknowledges that Figure 4 of Lipovsek presents a sequence alignment between a fibronectin type III protein domain

with sequences that are stated to be fibronectins from other sources, as well as sequences of related proteins. (See Figure 4, column 6, lines 31-33 and column 9, lines 9-12) The first row of Figure 4 depicts Hs FND (human fibronectin type III domain). Rows 2-9 depict alleged fibronectin sequences from other non-human sources (e.g., cow (row 2), rabbit (row 5), frog (row 7), dog (row 8) and horse (row 9). Rows 10-16 depicts sequences of other proteins (i. e., tenascin-C (row 10), tenascin precursor (row 11), collagen alpha precursor (row 13), collagen type 12 (row 14) and undulin 1 (row 16). Applicant initially submits that the sequences presented in rows 10-16 of Figure 4 of Lipovsek are not Fn3 molecules. Further, the only human sequence presented in rows 1-9 is the human fibronectin type III domain sequence itself. The other sequences presented in rows 2-9 are not human Fn3 sequences but instead are unmodified wild-type fibronectin sequences from other animals (e.g., cow, dog, horse, pig, rabbit or frog). Applicant submits that while the Board may have reasoned that certain Lipovsek sequences inherently anticipated the then pending claims, this information related to the sequences is relevant as to whether the instant claims are obvious in view of the Lipovsek sequences.

Appellant acknowledges that while amino acid residue 6 of the HsFND, Rn and Bt sequences is Arg, Applicant however submits

that none of HsFND or Rn or Bt comprise a substitution of at least one of amino acid residues 7, 9 or 23 with a neutral or positively charged amino acid residue.

Appellant submits that the Examiner has not demonstrated that it would be obvious to select a Lipovsek sequence that has an Arg at position 6 and to modify that sequence to arrive at Applicant's claimed invention, nor has the Examiner demonstrated that it would be obvious to select a Lipovsek sequence that comprises a substitution of at least one of amino acid residues 7, 9 or 23 with a neutral or positively charged amino acid residue and to modify that sequence to arrive at Applicant's claimed invention.

In reply, Fig. 4 of Lipovsek, as acknowledged by appellant, presents the alignment of the different wild type FN3 sequences common to the different mammalian species (see also col. 7, line 62 up to col.8, line 9). However, Lipovsek teaches, throughout the reference, a modified human FN3 (e.g., col. 2, lines 37-40 and col. 3, lines 45-55). Lipovsek teaches that the modified human FN3 has been altered by randomizing (col.4, lines 60-61) one or more amino acid residues with NNS wherein N is any of the four A, C, G and T and S is C or G (col. 18, lines 40-44 and col.12, lines 19-20) i.e., a positively, negatively charged and

neutral residues (col. 10, lines 17-25) thus including all the amino acids that fall under the broad neutral or positively charged residues. (For example if N is A and S is G (i.e., AAG) then the encoded amino acid is Lys. ACC is Asn. CGG is Arg and ATA for Ile and etc. Note that due to the degeneracy of the codons more than one amino acid can be encoded.)

Lipovsek teaches at col. 3, lines, 59-64, basic-neutral-acidic amino acid (albeit in the context of RGD present in Fn3) that can be replaced by other amino acids (e.g., Ser for Arg and Glu for Asp).

Lipovsek teaches at col. 9, lines 24-42 that the minimum residues that can be modified are the residues at 1-9 and 21-31 positions, inter alia (col. 9, lines 24-41) (encompassing the claim 7, 9 and 23 positions).

Lipovsek teaches at col. 7, lines 43-55 that these fibronectin-based (10FN3) scaffolds are **antibody mimics** which are similar in nature and affinity to those of antibodies, and a loop randomization and **shuffling** strategy may be employed in vitro that is similar to the process of affinity maturation of antibodies in vivo. [This is akin to the art known shuffling or replacing the human antibody sequence with amino acid residues from mouse that results in a hybridoma antibody].

Lipovsek teaches at e.g., col.9, lines 5-41:

> ….[F]ibronectins from other sources as well as sequences of related proteins (FIG. 4) and the **results of this alignment were mapped onto the three-dimensional structure of the human 10Fn3 domain (FIG. 5).** This alignment revealed that the majority of conserved residues are found in the core of the beta sheet sandwich, whereas the highly variable residues are located along the edges of the beta sheets, including the N- and C-termini, on the solvent-accessible faces of both beta sheets, and on three solvent-accessible loops that serve as the hypervariable loops for affinity maturation of the antibody mimics. **In view of these results, the randomization of these three loops are unlikely to have an adverse effect on the overall fold or stability of the 10 Fn3 framework itself..**(Emphasis added.)

Lipovsek teaches at col. 4, lines 46-53:

> ……….a fibronectin type III domain includes a sequence which exhibits at least 30% amino acid identity, and preferably at least 50% amino acid identity, to the sequence encoding the structure of the 10Fn3 domain….available from the Protein Data Base. Sequence identity referred to in this definition is determined by the Homology program….

The Board in their decision at page 11 states "[T]he PTO gives a disputed claim term its broadest reasonable interpretation during patent prosecution". In re Bigio, 381 F.3d 1320, 1324 (Fed. Cir. 2004). The court recognizes the fairness of reading claims broadly "before a patent is granted [since] the claims are readily amended as part of the examination process." Burlington Indus. v. Quigg, 822 F.2d 1581, 1583 (Fed. Cir. 1987). "Thus, a patent applicant has the opportunity and

responsibility to remove any ambiguity in claim term meaning by amending the application". Bigio, 381 F.3d at 1324. Applying the broadest reasonable interpretation to claims also "serves the public interest by reducing the possibility that claims, finally allowed, will be given broader scope than is justified." In re Am. Acad. Of Sci. Tech. Ctr., 367 F.3d 1359, 1364 (Fed. Cir. 2004).

The Specification does not directly define "modified" but discloses that a "stabilizing mutation is defined herein as a modification or change in the amino acid sequence of the Fn3 molecule, such as a substitution of one amino acid for another" (Spec. 6, lines 20-24). Also, the Specification states that "[o]ne or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3" (Spec. 7, lines 6-8; FF 15). Therefore, the word "modified" is reasonably interpreted in light of the Specification as representing a Fibronectin type III molecule in which there are one or more changes or substitutions in the amino acid sequence (relative to the human wild type sequence).

The specification (US Published Application No. 20030027319) defines the mutation of only Asp7 with Asn (neutral) or Lys(positively charged residue) in the context of the triad Asp 23 and Glu9 (the triad residues destabilizing FN3) (spec. at [0158]) "because Asp 7 is centrally located among the three residues, it was decided to mutate Asp 7. Two mutants were prepared, D7N and D7K (i.e., the aspartic acid at amino acid residue number 7 was substituted with an asparagine residue or a lysine residue, respectively). The former replaces the negative charge with a neutral residue of virtually the same size. The latter places a positive charge at residue 7."

The specification teaches at [0261] and Fig. 24:

> "These results clearly show that the repulsive interaction between D7 and D23 contributes to the increase in pKa of Asp 23 in the wild-type protein, and that it was eliminated by the neutralization of the negative charge at residue 7. The pKa of Glu 9 was reduced by the D7N mutation, while it was decreased in the D7K mutant. The greater reduction of Glu 9 pKa by the D7K mutation suggests that there is a favorable interaction between Lys 7 and Glu 9 in this mutant protein."

The specification does not specifically define the broad claim terms neutral or positively charged amino acid residues. The single residue asparagine (Asn) is defined as the neutral amino acid or Lys as positively charged residue. The mutant is

only made for Asp7 while Glu9 and Asp23 remain the same (or conservatively substituted with Asp for Glu9 but not as a positively charged residue for either Asp23 or Glu9).

The modified human Fn3 of Lipovsek with the residues replaced by NNS encoding specific amino acid residues encompassed by the broad claim positively or neutral residues anticipates the claim modified human Fn3. All the elements of the claim modified human Fn3 are identically disclosed by Lipovsek including the species of the broad claim neutral or positively charged residues. Or the modified Fn3(10Fn3) would be prima facie obvious as one can select from NNS the neutral or positively charged residue(s).

Furthermore, given the homology among the mammalian Fn3 species shown in Fig. 4, the sequences differ in one or more amino acids e.g., positions 7, 9 or 23; and its known mimic of antibody substitution one can readily envisage the claim modified human FN3. For example, one can replace the Asp7 in human Fn3 with the amino acid (asn) from the animal Fn3, Cf and/or Ec and reasonably expect the stability of the human Fn3 to remain. [It is of interest to note that in Fig. 4, the lower case residues such as n (Asn) for Cf or Ec at position 7 and r (arg) at position 9 are taught by Lipovsek to be non-

conservative substitutions (i.e., charge reversal or change between hydrophobic and charged residue). The BOLD residue(s) is taught to be identical to human Fn3. LEU shown at the bottom alignment at position 7 is presumed to have replaced Asp (as per the mapping taught by Lipovsek above.)]

Appellant moreover argues that the Board has previously determined that "the Examiner erred in finding it obvious to modify Asp7, Asp23 or Glu9 on the Fibronectin type III scaffolds of Koide and Lipovsek based on the teachings of Spector." (see page 8 of the June 9, 2009 Decision on Appeal).

In reply, the above rejection is based on Lipovsek alone and not on the combined teachings of Lipovsek, Koide and Spector references as decided by the Board in the then pending claims.

<u>Claim 80</u>

Appellant states that claim 80 is directed to a modified human Fn3 molecule comprising a stabilizing mutation of at least one residue involved in an unfavorable electrostatic interaction as compared to the wild-type human Fn3, wherein the stabilizing mutation is a substitution of Asp 7 or Asp 23 with a positively

charged amino acid residue. At page 10 of the Office Action, the Examiner does not respond to Applicant’s previous argument that such Fn3 molecules are anticipated by nor obvious in view of Lipovsek by stating "please see the rejection above, addressing all of these different substitutions including Asp 7 or Asp 23 substituted with asn." Applicant respectfully disagrees with the Examiner's conclusions at page 11 of the final Office Action that "Lipovsek presents said alignment of sequences that are homologous to HsFND such that substitution of one sequence with another in aligned sequences that are homologs of HsFND can be made" and that it "would be within the ordinary skill in the art given the homologous sequences to substitute one residue with another residue with a reasonable expectation that such substitutions will result in a stabilized molecule as taught by Lipovsek. It could not be otherwise." The Board has previously determined that "the Examiner erred in finding it obvious to modify Asp7, Asp23 or Glu9 on the Fibronectin type III scaffolds of Koide and Lipovsek based on the teachings of Spector." (see page 8 of the June 9, 2009 Decision on Appeal) Accordingly, Applicant submits that such modifications would not be obvious to the art worker.

In reply, claim 80 defines replacing only Asp 7 or 23 with a positively charged amino acid residue. The rejections above also apply herein as follows:

In reply, Fig. 4 of Lipovsek, as acknowledged by appellant, presents the alignment of the different wild type FN3 sequences common to the different mammalian species (see also col. 7, line 62 up to col.8, line 9). However, Lipovsek teaches, throughout the reference, a modified human FN3 (e.g., col. 2, lines 37-40 and col. 3, lines 45-55). Lipovsek teaches that the modified human FN3 has been altered by randomizing (col.4, lines 60-61) one or more amino acid residues with NNS wherein N is any of the four A, C, G and T and S is C or G (col. 18, lines 40-44 and col.12, lines 19-20) i.e., a positively, negatively charged and neutral residues (col. 10, lines 17-25). (For example if N is A and S is G (i.e., AAG) then the encoded amino acid is Lys. ACC is Asn. CGG is Arg and ATA for Ile and etc. Note that due to the degeneracy of the codons more than one amino acid can be encoded.)

Lipovsek teaches at col. 3, lines, 59-64, basic-neutral-acidic amino acid (albeit in the context of RGD present in Fn3) that can be replaced by other amino acids (e.g., Ser for Arg and Glu for Asp).

Lipovsek teaches at col. 9, lines 24-42 that the minimum residues that can be modified are the residues at 1-9 and 21-31 positions, inter alia (col. 9, lines 24-41) (encompassing the claim 7, 9 and 23 positions).

Lipovsek teaches at col. 7, lines 43-55 that these fibronectin-based (10FN3) scaffolds are **antibody mimics** which are similar in nature and affinity to those of antibodies, and a loop randomization and **shuffling** strategy may be employed in vitro that is similar to the process of affinity maturation of antibodies in vivo. [This is akin to the art known shuffling or replacing the human antibody sequence with amino acid residues from mouse that results in a hybridoma antibody].

Lipovsek teaches at e.g., col.9, lines 5-41:

> ….[F]ibronectins from other sources as well as sequences of related proteins (FIG. 4) and the **results of this alignment were mapped onto the three-dimensional structure of the human 10Fn3 domain (FIG. 5).** This alignment revealed that the majority of conserved residues are found in the core of the beta sheet sandwich, whereas the highly variable residues are located along the edges of the beta sheets, including the N- and C-termini, on the solvent-accessible faces of both beta sheets, and on three solvent-accessible loops that serve as the hypervariable loops for affinity maturation of the antibody mimics. **In view of these results, the randomization of these three loops are unlikely to have an adverse effect on the overall fold or stability of the 10 Fn3 framework itself..**(Emphasis added.)

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modification or change in the amino acid sequence of the Fn3 molecule, such as a substitution of one amino acid for another" (Spec. 6, lines 20-24). Also, the Specification states that "[o]ne or more of the monobody loop region sequences of the Fn3 polypeptide vary by deletion, insertion or replacement of at least two amino acids from the corresponding loop region sequences in wild-type Fn3" (Spec. 7, lines 6-8; FF 15). Therefore, the word "modified" is reasonably interpreted in light of the Specification as representing a Fibronectin type III molecule in which there are one or more changes or substitutions in the amino acid sequence (relative to the human wild type sequence).

The specification (US Published Application No. 20030027319) defines the mutation of only Asp7 with Asn (neutral) or Lys(positively charged residue) in the context of the triad Asp 23 and Glu9 (the triad residues destabilizing FN3) (spec. at [0158]) "because Asp 7 is centrally located among the three residues, it was decided to mutate Asp 7. Two mutants were prepared, D7N and D7K (i.e., the aspartic acid at amino acid residue number 7 was substituted with an asparagine residue or a lysine residue, respectively). The former replaces the negative

charge with a neutral residue of virtually the same size. The latter places a positive charge at residue 7."

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The specification does not specifically define the broad claim terms neutral or positively charged amino acid residues. The single residue asparagine (Asn) is defined as the neutral amino acid or Lys as positively charged residue. The mutant is only made for Asp7 while Glu9 and Asp23 remain the same (or conservatively substituted with Asp for Glu9 but not as a positively charged residue for either Asp23 or Glu9).

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Lipovsek including the species of the broad claim neutral or positively charged residues. Or the modified Fn3(10Fn3) would be prima facie obvious as one can select from NNS the neutral or positively charged residue(s).

Furthermore, given the homology among the mammalian Fn3 species shown in Fig. 4, the sequences differ in one or more amino acids e.g., positions 7, 9 or 23; and its known mimic of antibody substitution one can readily envisage the claim modified human FN3. For example, one can replace the Asp7 in human Fn3 with the amino acid (asn) from the animal Fn3, Cf and/or Ec and reasonably expect the stability of the human Fn3 to remain. [It is of interest to note that in Fig. 4, the lower case residues such as n (Asn) for Cf or Ec at position 7 and r (arg) at position 9 are taught by Lipovsek to be non-conservative substitutions (i.e., charge reversal or change between hydrophobic and charged residue). The BOLD residue(s) is taught to be identical to human Fn3. LEU shown at the bottom alignment at position 7 is presumed to have replaced Asp (as per the mapping taught by Lipovsek above.)]

Further the specification teaches only the mutants for Asp7 while keeping Asp 23 and Glu9 intact so as to stabilize Fn3 (not Asp23 replaced by positively charged residue). In light of the

specification teachings, Lipovsek’s teachings of replacing amino acid at position 23 with Glu, a known conservative substitution included in the defined NNS encoded amino acid fully meets all the elements of the broad claimed modified human Fn3. Or is prima facie obvious in the selection of the NNS specifically encoded amino acid residues encompass by the claim neutral or positively charged residues.

Appellant argues that the Board has previously determined that "the Examiner erred in finding it obvious to modify Asp7, Asp23 or Glu9 on the Fibronectin type III scaffolds of Koide and Lipovsek based on the teachings of Spector." (see page 8 of the June 9, 2009 Decision on Appeal).

In reply, the above rejection is based on Lipovsek alone and not on the combined teachings of Lipovsek, Koide and Spector references as decided by the Board in the then pending claims.

(11) Related Proceeding(s) Appendix

Copies of the court or Board decision(s) identified in the Related Appeals and Interferences section (of this same

application) of this examiner's answer are provided herein by appellant.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1636

Conferees:

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1636

/Peter Paras, Jr./

Supervisory Patent Examiner, Art Unit 1632